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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,102	07/25/2003	Michael William Dunne	PC 23140A (121*399)	3522

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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,102	DUNNE, MICHAEL WILLIAM	
	Examiner	Art Unit	
	Traviss C McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-147* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-147* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/25/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Specification

The abstract of the disclosure is objected to because the abstract's content fails to enable the reader thereof, regardless of his or her degree of familiarity with patent documents, to quickly ascertain the character of the subject matter covered by the technical disclosure and fails to include that which is new in the art to which the invention pertains.

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, *e.g.*, "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Complete revision of the content of the abstract is required on a separate sheet.

Claim Objections

Applicant is advised that should claim 20 be found allowable, claims 30, 50, 70, and 130 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

In the instant case, all of claims 20, 30, 50, 70, and 130 are drawn to treating acute otitis media comprising administering to a human in need thereof a single dose of Azithromycin wherein the dose is about 30 mg/kg body weight or greater.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-147 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of acute otitis media and bacterial infections in patients comprising administering a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater (or 0.15-4.5 g), does not reasonably provide enablement for treating any respiratory infection comprising administering a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater (or 0.15-4.5 g). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:
(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Independent claims 1 and 21 are drawn to treating any respiratory infection comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater (0.15-4.5 g). Independent claim 28 is drawn to treating any respiratory infection caused by *S. pneumoniae* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 68 is drawn to treating any respiratory infection caused by *H. influenzae* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 88 is drawn to treating any infection caused by *S. pyogenes* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 108 is drawn to treating any infection caused by *E. faecalis* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 128 is drawn to treating any respiratory infection caused by *M. catarrhalis* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Dependent claims limit the independent claim's dosage

amounts to various ranges, limit the patient to that of a human 16 years old or older, and limit the infection to acute otitis media.

The state of the prior art

Azithromycin is known in the art to be beneficial as a broad-spectrum antibiotic as evidenced by Dawson et al. (US Patent 6,569,443 – column 3, lines 57+). Respiratory infections are known to be caused by agents other than bacteria, such as by viral infections or fungal infections, which are not normally successfully treated with antibacterial agents (see Park et al. 2004/0053264, paragraph 54). Moreover, macrolides are known to be administered in various amounts depending on various factors, including route of delivery, age of patient, sex of patient, weight of patient, etc. At present, there is no known agent capable of effectively treating every respiratory infection caused by any organism or infection caused by any organism.

The level of predictability in the art

The examiner acknowledges the probability and predictability that the active agent, which is azithromycin, indeed has efficacy in treating bacterial infections, and bacterial infections causing acute otitis media, comprising administering a dose of about 30 mg/kg body weight or higher, however the art is silent with regard to the predictability of effectively treating any respiratory infection with the instantly claimed therapy.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written. The examiner notes, there has not been

provided sufficient instruction or sufficient methodological procedures to support the alleged efficacy of treating any respiratory infection in any patient as instantly asserted.

The existence of working examples

The working examples set forth in the instant specification are drawn to the following examples:

Example 1: single dose Azithromycin test on patients from 6 months – 12 years old wherein patients with acute otitis media (and which had a pathogen identified at baseline culture being one of: *M. catarrhalis, S. pneumonia, or H. influenzae*) were treated. It is noted there were no control groups shown.

Example 2: various experiments showing the effect of dose regimen of azithromycin and clarithromycin to determine the protective dose amount in various murine models wherein the following pathogens were tested against: *S. pyogenes, H. influenzae, M. catarrhalis, E. faecalis*, and *S. pneumoniae* (with and without mef A gene).

Example 3: various experiments showing an accelerated dosing paradigm in the gerbil middle ear infection model infected with various strains of *H. influenzae* using azithromycin in various doses and regimens.

Example 4: various experiments showing an accelerated dosing paradigm in various models infected with *S. pneumoniae, S. pyogenes, E. faecalis,* and various strains of *H. influenzae* using azithromycin and clarithromycin various doses and regimens.

Example 5: a non-comparative study on pediatric subjects undergoing diagnostic tympanocentesis comprising administering a single 30 mg/kg dose of azithromycin.

There has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that any individual with any respiratory infection would be effectively treated with the instantly claimed therapy.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable the use of the instantly claimed therapy without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 20, 22, 30, 50, 70, and 130 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

All of these claims, 20, 22, 30, 50, 70, and 130, intend to limit the "respiratory infection" in the claims from which they depend to "acute otitis media", however, acute otitis media is not a respiratory infection. Acute otitis media is an infection of the area behind the eardrum in the middle ear that produces pus, fluid, and inflammation within the middle ear, as well as symptoms which are frequently associated with signs of upper respiratory infection, such as a runny nose or cough and the period of incubation is variable, but usually otitis media is preceded by 4-7 days of

upper respiratory tract infection (as seen in "Ear Infections (Otitis Media)" from Kids Health). The attempt to limit a respiratory infection to acute otitis media (an ear infection) is confusing.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-2, 5-8, 20-23, 28, 30-31, 34-37, 48, 50-51, 54-57, 68, 70-71, 74-77, 128, 130-131, and 134-137 are rejected under 35 U.S.C. 102(a) as being anticipated by P/S/L Consulting Group (Ref. AM of IDS).

Claim 1 is drawn to a method of treating a respiratory infection in a human comprising administering a single dose of azithromycin of about 30 mg/kg body weight or greater to said human. Claim 2 provides the dose is about 31 mg/kg body weight or greater. Claims 5-8 provide various dosage ranges which are all have the lower limit of the range as about 30-35 mg/kg body weight. Claim 20 provides that the infection is acute otitis media. Claim 21 is drawn to the same method as claim 1, except the dosage is set forth as about 0.15-4.5 g. Claim 22 limits claim 21 wherein the infection is acute otitis media. Claim 23 limits the dose of claim 21 to about 0.15-1.5 g. Independent claim 28 is drawn to treating a respiratory infection caused by *S. pneumoniae* following the method of claim 1. Claims 30-31 and 34-37 limit claim 28 in the same manner that claims 20, 2, and 5-8 limit claim 1 respectively. Independent claim 48 is drawn to treating a

respiratory infection caused by *S. pneumoniae* containing a mef A gene following the method of claim 1. Claims 50-51 and 54-57 limit claim 48 in the same manner that claims 20, 2, and 5-8 limit claim 1 respectively. Independent claim 68 is drawn to treating a respiratory infection caused by *H. influenzae* following the method of claim 1. Claims 70-71 and 74-77 limit claim 68 in the same manner that claims 20, 2, and 5-8 limit claim 1 respectively. Independent claim 128 is drawn to treating a respiratory infection caused by *M. catarrhalis* following the method of claim 1. Claims 130-131 and 134-137 limit claim 128 in the same manner that claims 20, 2, and 5-8 limit claim 1 respectively.

The P/S/L article discloses a single-dose regimen as an option for children with acute otitis media comprising 30 mg/kg of azithromycin. Moreover, it is disclosed that azithromycin is indicated for acute otitis media caused by *S. pneumoniae, H. influenzae, and M. catarrhalis* (see entire document). Thus, the present invention is drawn to treating the aforementioned conditions comprising a single dose therapy of about 30 mg/kg body weight, and the P/S/L document discloses treating the same conditions in the same populations, using the same compound in the same amount. Moreover, it is noted that the lower limit as claimed as being "about 35 mg/kg" is seen to be anticipated by the teaching of 30 mg/kg, as the examiner has interpreted the 30 mg/kg taught to be about 35 mg/kg.

Claims 1-2, 5-8, and 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Block et al. (reference Al of IDS).

Claims 1-2, 5-8, and 20-23 are drawn to methods of treatment as set forth supra.

Block et al. disclose methods of treating acute otitis media in pediatric patients comprising administering a single dose of azithromycin in an amount of 30 mg/kg).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determining the scope and contents of the prior art.
Ascertaining the differences between the prior art and the claims at issue.
Resolving the level of ordinary skill in the pertinent art.
Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-147 are rejected under 35 U.S.C. 103(a) as being unpatentable over the P/S/L document as set forth supra in combination with Lazarevski et al. (US Patent 6,110,965).

Independent claims 1 and 21 are drawn to treating any respiratory infection comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater (0.15-4.5 g). Independent claim 28 is drawn to treating any respiratory infection caused by *S. pneumoniae* (claim 48 provides *S. pneumoniae* with a mef A gene) in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 68 is drawn to treating any

respiratory infection caused by *H. influenzae* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 88 is drawn to treating any infection caused by *S. pyogenes* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 108 is drawn to treating any infection caused by *E. faecalis* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Independent claim 128 is drawn to treating any respiratory infection caused by *M. catarrhalis* in a human comprising administering to a human a single dose of azithromycin wherein the dose is about 30 mg/kg body weight or greater. Dependent claims limit the independent claim's dosage amounts to various ranges, the patients to above 16 years of age, and limit the infection to acute otitis media.

The P/S/L article discloses a single-dose regimen as an option for children with acute otitis media comprising 30 mg/kg of azithromycin. Moreover, it is disclosed that azithromycin is indicated for acute otitis media caused by *S. pneumoniae, H. influenzae, and M. catarrhalis* (see entire document). The P/S/L document discloses treating various bacterial infections in the same populations, using the same compound in the same amount. Moreover, it is noted that the lower limit as claimed as being "about 35 mg/kg" is seen to be anticipated by the teaching of 30 mg/kg, as the examiner has interpreted the 30 mg/kg taught to be about 35 mg/kg. Moreover, the P/S/L document teaches that azithromycin is approved for use in children and adults. What is not taught is the treatment of *S. pyogenes* or *E. faecalis* related infections, nor the various dosages of 40-90 mg/kg body weight.

Lazarevski et al. is cited to show that azithromycin is effective against *S. pyogenes* and *E. faecalis* (see table 1, column 8).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the method disclosed in the P/S/L document to treat bacterial infections from *S. pyogenes* or *E. faecalis* as Lazarevski et al. teach that azithromycin is effective against the various pathogens. Moreover, it would be obvious to vary the dosage, as azithromycin is this is seen as optimization of an art known method. One of skill in the art would be appraised of methods of determining the optimum dosages of the compound using art recognized procedures. One would be motivated to treat the various bacterial infections from *S. pyogenes* or *E. faecalis* using the method of the P/S/L document because azithromycin is known to be effective in various dosages against various bacterial pathogens, and the P/S/L document shows that the results of their study indicate that a single oral dose of the medication can accomplish what traditionally has taken up to 10 days.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh III
April 27, 2004